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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,516	03/01/2002	Xuanchuan Yu	LEX-0316-USA	6467

24231 7590 01/09/2004

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,516	YU ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 9-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 9-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ *Certified copies of the priority documents have been received in Application No.* _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

[1] Claims 1, 3-5, and 9-13 are pending in the application.

[2] Applicants' amendment to the claims filed October 15, 2003, is acknowledged. This listing of the claims replaces all previous versions and listings of the claims in the instant application.

[3] Applicants' confirmation of the election of Group I, original claims 1-6, without traverse, is acknowledged.

[4] Applicants' arguments filed October 15, 2003 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Objections

[6] In view of applicants' amendment to the claims filed October 15, 2003, the objections to claims 2-3 and 5-6 as set forth in items 14-17 of the Office action mailed June 09, 2003, are withdrawn.

Claim Rejections - 35 USC § 112, Second Paragraph

[7] In view of applicants' amendment to the claims filed October 15, 2003, the rejection of claim 2 as set forth in item 18 of the Office action mailed June 09, 2003, is withdrawn. It is noted that applicants state claim 5 is also rejected under this statute and the Office action provides no details regarding the rejection of this claim. The rejection under 35 USC 112, second paragraph, as set forth in the file copy of the Office action does not reject claim 5 and it appears this may have been an editing error that resulted in a rejection of claims 2 and 5 under 35 USC 112, second paragraph, in applicants' copy of the Office action. In order to clarify the record, it is noted that only claim 2 should have been rejected under 35 USC 112, second paragraph, in the Office action mailed June 09, 2003. Claim 5 should NOT have been rejected under 35 USC 112, second paragraph, in that Office action.

Claim Rejections - 35 USC § 101

[8] The utility rejection of claims 1, 3-5, and 9-13 under 35 USC § 101 is maintained for the reasons of record as set forth in item 19 of the Office action mailed June 09, 2003 and for the reasons stated below. Applicants argue (beginning at the top of page 6 of the response) the invention has numerous substantial and credible utilities such as use in forensic biology. Applicants argue the specification describes a number of single nucleotide polymorphisms (SNPs) in the sequence of SEQ ID NO:1 and 3 (page 19 of the specification). Applicants argue such SNPs are the basis for forensic analysis, which is allegedly a "real world" use and assert that the disclosed sequences must therefore be useful. Applicants argue the polymorphisms need not be related to a disease state in order to be used in forensic analysis to identify individual members of the human population based on the presence or absence of the described polymorphisms. Applicants argue (page 7, top of the response) that, at worst, each polymorphism is useful to distinguish 50% of the population and the ability to eliminate 50% of the population is clearly a real world use. Applicants' argument is not found persuasive.

The examiner acknowledges that the specification discloses SNPs. However, the specification fails to provide guidance for using any of the disclosed SNPs to "distinguish members of a population from one another" as asserted by applicants. For example, the frequency of any single polymorphism is highly variable and the specification fails to characterize the occurrence of any of the described polymorphisms in the human population. It should be noted that, while applicants assert, "each marker is useful to distinguish 50% of the population" (page 5 of the response), there is no evidence of record that would indicate or even suggest that any of the polymorphisms has a 50% frequency of occurrence. Also, the specification fails to provide a correlation of the SNPs with any subpopulation (e.g., African-American, Asian, and/or Caucasian) such that the polymorphisms may be used to distinguish a subpopulation from the general population. Furthermore, even assuming *arguendo* that the frequency of the disclosed polymorphisms was established in a given subpopulation, unless the polymorphism is *specific* for that subpopulation, there is no way to distinguish a subpopulation from any other population. For at least the reasons given above, it is unclear as to what useful information can be derived from or how one would

interpret a result from genotyping a DNA sample using the claimed polynucleotide to detect the presence or absence of the disclosed polymorphisms. In this case, further experimentation is required to establish a "real world" use for the claimed polynucleotides. This further experimentation however is part of the act of invention and until it has been undertaken, applicants' invention is incomplete. Therefore, the claimed polynucleotide has no substantial utility.

Beginning at the top of page 7 of the response, applicants argue that the examiner's assertion that the asserted utilities apply to the broad class of nucleic acids has two flaws. First, applicants argue not all nucleic acids contain polymorphic markers and these markers are specific and unique to a subset of the population. Applicants argue the examiner appears to be attempting to use applicants' disclosure as hindsight verification that the claimed sequence would be expected to have a polymorphism and this is improper. Second, applicants argue there is no requirement that the invention have a unique utility. Applicants' arguments are not found persuasive.

As previously stated, the examiner acknowledges that the specification discloses SNPs in SEQ ID NO:1 and 3 (page 19 of the specification). While it is acknowledged that the SNPs as described in the specification are specific to SEQ ID NO:1 and 3, as stated above, further experimentation is required to establish a "real world" use for the claimed invention. For example, what useful information can be derived from genotyping a DNA sample using the claimed polynucleotide to detect the presence or absence of the disclosed polymorphism? In this case, further experimentation would be required to interpret such a result and therefore, the invention has no substantial utility. Regarding the asserted requirement of a unique utility, it is noted that applicants have never been asked to identify a utility that is unique, i.e., not shared by any other compounds or compositions. Rather, applicants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. An invention certainly can have a utility that is shared by other compounds or compositions. On the other hand, not every utility will satisfy 35 USC § 101, even if the utility is shared by a class of inventions. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101. Here, applicants

assert that the claimed polynucleotides can be used in forensic analysis. However, as stated above, any results of genotyping of a nucleic acid sample would have no meaning without additional experimentation.

Beginning at the middle of page 8 of the response, applicants argue the disclosed SNPs are part of "the family of polymorphisms that have a well established utility" and cite *In re Brana* as allegedly supporting their argument. Applicants reiterate their argument that the polymorphic markers can distinguish members of a population from one another. Applicants argue that even if further research is required on the percentage of particular subpopulations that possess the polymorphism, this does not preclude a finding that the invention has patentable utility and cite *In re Brana* as allegedly supporting their argument. Applicants argue the need for some experimentation does not render the invention unpatentable and that a considerable amount of experimentation may be permissible if routine. Applicant's argument is not found persuasive.

It should be noted that the claimed invention is a polynucleotide encoding SEQ ID NO:2 and 4, including SEQ ID NO:1 and 3, respectively. Applicants' arguments (in part) are directed to the utility of the SNPs and not the claimed invention, i.e., the claimed invention is not the disclosed polymorphisms. Furthermore, contrary to applicants' assertions, there is no evidence of record that the disclosed SNPs have a well-established utility. As previously stated, further experimentation is required to establish a "real world" use for the claimed polynucleotides for use in forensic analysis and thus, there is no well-established utility for the claimed polynucleotides. In *Brana,* the claimed invention was shown to have patentable utility based on evidence provided in the specification demonstrating *in vitro* anticancer activity of the claimed compound. Thus, the court found the claimed invention to have patentable utility based on the asserted "antitmour activity". The court's statement regarding "the expectation of further research and development" was directed to Phase II experiments to confirm antitumor activity *in a human,* however, it should be noted that no further experimentation was required to confirm the utility of the claimed invention for the asserted use disclosed in the specification, i.e., the claimed invention was useful in a currently available form without need for further experimentation. Contrary to *In re Brana,* the instant specification fails to provide sufficient guidance to enable one of skill in the art to use the claimed invention to "distinguish members of a population from one another" as asserted by applicants. For example, as

stated above, the specification fails to provide guidance for interpreting any result obtained from genotyping a nucleic acid sample for the presence or absence of the disclosed polymorphism.

Applicants argue (beginning at the bottom of page 9 of the response) that a statement of utility must be accepted absent reasons why a skilled artisan would doubt the truth of such statement. Applicants argue absent such evidence, one of ordinary skill in the art would understand the polymorphisms have utility in forensic analysis. Applicant's argument is not found persuasive.

Applicants' arguments appear to address the issue of credibility of an asserted utility. However, the examiner has not questioned the credibility of applicants' asserted use of the claimed polynucleotides for detecting the presence or absence of a polymorphism. In this case, the rejection is based on the specification's failure to disclose a specific and substantial asserted utility – not the absence of a credible utility.

Applicants argue (beginning at the top of page 10 of the response) that the claimed sequence shares greater than 96% sequence identity with two GenBank sequences that have been independently annotated as Ten-m4. Applicants argue that based on this evidence, there can be no question that those skilled in the art would believe the claimed sequence is a human Ten-m4 protein variant, as asserted by applicants. Applicants argue (beginning at the middle of page 10 of the response) that in view of the relatively high degree of sequence identity, the instant situation is similar to Example 10 of the Revised Interim Utility Guidelines Training Materials that states that a utility rejection is not proper when a full-length sequence has a similarity score >95% to a protein of known function. Applicants' argument is not found persuasive.

It should be noted that applicants' assertion that the claimed sequence is a human Ten-m4 protein variant is acknowledged, however, while the title suggests that SEQ ID NO:2 and 4 and polynucleotides encoding therefor are human Ten-m4/cdz proteins, there is no assertion that the proteins of SEQ ID NO:2 and 4 have Ten-m4/cdz protein activity. Instead, the specification indicates that SEQ ID NO:2 and 4 "share structural similarity" with proteins that appear to have distinct biological activities- 1) murine Ten-m4/cdz and 2) proteins identified as gamma-heregulins (see page 2, lines 5-11 of the instant specification). In this case, the specification discloses that SEQ ID NO:2 and 4 have similarity to proteins

which appear to have distinct biological activities - Ten-m4/cdz and gamma-heregulin proteins. As such, further experimentation would at least be required to determine which of the two biological activities was exhibited by SEQ ID NO:2 and 4 in order to establish a "real world" use for the claimed sequences. Even assuming *arguendo* applicants' specification expressly disclosed that SEQ ID NO:2 and 4 function as Ten-m4/cdz proteins (whatever "function" that may be as the prior art does not define such function and Oohashi et al. state, "it is not clear which function is propagated by this protein"), despite applicants' evidence, *i.e.,* 96% sequence identity to another Ten-m4/cdz protein, no more is known about the function of SEQ ID NO:2 and 4 than in the absence of the evidence. In this case, applicants attempt to demonstrate function *in silico,* by mere similarity to another protein sequence. One of skill in the art recognizes that only by empirical characterization can the function of a protein be ascertained (see, *e.g.,* Brenner and Scott et al.). In this case, applicants have made a strong assumption that the polypeptides of SEQ ID NO:2 and 4 have *any* biological activity. However, there is no evidence of record to suggest that the polypeptides of SEQ ID NO:2 and 4 have *any* biological function and it is just as likely that the polypeptides of SEQ ID NO:2 and 4 have no function, i.e., they are non-functional polypeptides. Thus, further experimentation would be required to establish whether SEQ ID NO:2 and 4 have *any* biological function or more particularly the "function" of a Ten-m4/cdz protein – whatever that may be. Even assuming *arguendo* that SEQ ID NO:2 and 4 has Ten-m4/cdz "function", further experimentation is required to establish a "real world" use of the claimed sequences. In this case, based on the vague characterization of Ten-m4/cdz as a stress-response protein (Wang et al. and Oohashi et al.), one of skill in the art would not recognize the biological significance of the claimed sequences and would not be able to use the claimed invention in currently available form. Also, contrary to applicants' assertion, the instant case is not similar to Example 10 of the Revised Interim Utility Guidelines Training Materials. Example 10 of the training materials states that the encoded protein, which shares 95% sequence identity to other ligases, is asserted to be a DNA ligase and DNA ligases have a well-established utility in molecular biology. In the instant case, the specification makes no assertion of the biological activity of SEQ ID NO:2 and 4 and indicates only that SEQ ID NO:2 and 4 share structural similarity with two proteins that appear to have distinct biological functions. Furthermore, even if SEQ ID NO:2 and 4 have Ten-m4/cdz "activity",

the prior art does not define such activity (see page 6, bottom to page 7 top of item 19 of the Office action mailed June 09, 2003), and the skilled artisan is left to experiment in order to identify the biological significance of the encoding nucleic acids.

At the bottom of page 10 of the response, applicant argues that given the well-established role of ten-m proteins in development (citing Feng et al. and Oohashi et al.), an additional example of utility is tracking expression of the claimed sequences using DNA chips. Applicants argue that since the sequences are markers of human chromosome 11, a skilled artisan would recognize the claimed sequences would be an "ideal, novel candidate" for use in gene expression analysis with DNA chips. Applicants argue that due to the widespread utility of gene chips using public domain gene information, there can be little doubt that the claimed sequences would have utility in DNA chip applications. Applicants argue that compositions that enhance the utility of such DNA chips must themselves be useful. Applicants' argument is not found persuasive.

It should be noted that the reference of Feng et al. was not available at the time of filing of the instant application and the reference of Oohashi et al. states that it is not clear as to the biological activity of Ten-m4 (see page 573, right column, bottom). Thus, one of ordinary skill in the art would not recognize the so-called "well-established" role of ten-m proteins in development. Regarding the asserted utility of the claimed sequences in gene expression monitoring using gene chips, it is noted that any sequence can be included as a component of a gene chip, *e.g.*, as a chromosomal marker. This utility is not specific to the claimed sequences and instead applies to the general class of nucleic acids as evidence by applicants' own statement regarding the widespread use of such gene chips using public domain gene sequences. It is also noted that the claims are drawn to polynucleotide sequences – not to the physical DNA chip itself or methods of use thereof. Furthermore, any information derived from gene expression analysis using the claimed sequences would be meaningless as the specification fails to provide guidance for interpreting any result obtained thereby.

Beginning at the middle of page 11 of the response, applicants argue that evidence of "real world" substantial utility, is further provided by the fact that there is an entire industry established based on the use of gene sequences in DNA chip format. Applicants argue that the use of gene sequences is a "real

world" substantial, widespread and well-established utility. Applicants argue that the utility of genomic data, and specifically human genomic data is well recognized and cite Venter et al. and Jasny et al. as allegedly supporting their argument. Applicant's argument is not found persuasive.

Evidence of commercial success, while sometimes persuasive as secondary evidence of non-obviousness, is immaterial to utility and enablement. Many products have enjoyed commercial success due to fads or clever advertising, wherein the products would not have met the legal standards for utility under 35 USC § 101. In this case, there is no dispute as to the potential usefulness of information obtained from the sequencing of the human genome. However this information is valuable to the extent that it provides a starting point for scientists to further investigate the biological significance of the genetic information collected. In the absence of any information as to the interpretation of a result obtained by gene expression analysis using a DNA chip, the claimed sequences are useful only for further experimentation to investigate their biological significance. As such, the asserted utility of gene expression analysis is not a substantial utility. It should be noted that the issue at hand is the utility of the claimed sequences and not DNA chips or methods of use thereof. In the instant case, applicants have failed to demonstrate a patentable utility for the claimed invention.

Beginning at the top of page 12 of the response, applicants argue the examiner's assertion that the use of sequences in gene expression monitoring is flawed in two respects: 1) only expressed sequences can be used to track gene expression and 2) applicants reiterate their argument that the examiner has confused the requirements for a specific utility with a unique utility. Applicant's argument is not found persuasive.

The asserted utility of using the claimed sequences is neither specific nor substantial. *Any* expressed or non-expressed sequence can be used for gene expression monitoring – this utility is not specific. In this case the information provided by gene expression analysis is meaningless (as described in detail above) as the specification fails to provide any guidance as to how one would interpret data obtained from such an analysis. Regarding a unique utility, as previously stated, applicants mischaracterize the examiner's position as applicants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties

of the claimed invention. An invention certainly can have a utility that is shared by other compounds or compositions. On the other hand, not every utility will satisfy 35 USC § 101, even if the utility is shared by a class of inventions. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101. Here, applicants assert that the claimed polynucleotides can be used in gene expression analysis. However, as stated above, any results obtained thereby would have no meaning without additional experimentation.

At the middle of page 12 of the response applicants argue the claimed invention has a specific utility in identifying coding sequence and chromosomal mapping. In applicants' opinion, the claimed sequences provide "exquisite specificity" in localizing the specific region of human chromosome 11 and that this specificity is useful because it is allegedly shared by virtually no other sequences. Applicants' argument is not found persuasive.

Any expressed human polynucleotide, *e.g.,* a cDNA, can be used to detect a particular locus of the corresponding gene, therefore *any* human polynucleotide which encodes a protein can be used to determine the specific chromosome which contains that locus. Regarding identification of a *specific* region of human chromosome 11 using the claimed sequences, it is noted that, at the time of filing of the instant application, there was no evidence of record or line of reasoning to suggest that the claimed sequences were useful for identifying any specific region of chromosome 11 or that the region comprising the claimed sequences was shared by virtually any other nucleic acids. Based on the specification, this would have required further experimentation and thus, this utility would not be substantial. In regard to the use of the claimed polynucleotides in producing a genetic map of high resolution, it is noted that this use is not specific since many other expressed polynucleotides as indicated above can be used in a similar way. In this case, the asserted utilities are applicable to the broad class of nucleic acids sequences.

At the top of page 12 of the response, applicants argue that since only a minor portion of the genome contains exons, the claimed polynucleotides provide biologically validated empirical data that specifically define that portion of the genomic locus that actually contains an exon. Applicants further argue that the claimed polynucleotides define how exons are spliced to produce an active transcript. Applicants argue that since their polynucleotides define biologically validated empirical data, the present

claims meet the requirements of 35 USC §101. For a third time, applicants reiterate their argument that the examiner has confused the requirements for a specific utility with a unique utility. Applicants' arguments are not found persuasive.

As previously stated, the asserted utilities are not specific to the claimed invention as all expressed polynucleotides have such utilities. Such utilities do not meet the specific and substantial requirements of 35 USC § 101. Regarding a unique utility, as previously stated, applicants mischaracterize the examiner's position as applicants have been required to identify a utility that is specific to the invention claimed, as opposed to one that would apply regardless of the specific properties of the claimed invention. An invention certainly can have a utility that is shared by other compounds or compositions. On the other hand, not every utility will satisfy 35 USC § 101, even if the utility is shared by a class of inventions. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101. Here, applicants assert that the claimed polynucleotides can be used in gene expression analysis. However, as stated above, any results obtained thereby would have no meaning without additional experimentation.

At the bottom of page 13 of the response, applicants argue that the Federal Circuit in *Juicy Whip Inc. v. Orange Bang, Inc.* has stated that the threshold of utility is not high and that an invention is useful under § 101 if it is capable of providing some identifiable benefit. Applicants further cite *Brooktree Corp. v. Advanced Micro Devices, Inc.* to indicate that the Federal Circuit has stated that a claimed device must be totally incapable of achieving a useful result to lack utility under 35 USC § 101. Applicants cite *Cross v. Iizuka* in support of their argument that any utility for a claimed invention is sufficient to satisfy the requirements of 35 USC § 101 and indicate that the Federal Circuit has confirmed that anything "under the sun" made by man is patentable in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.*

It is noted that only *Cross v. Iizuka* is considered relevant to the instant discussion since the inventions in that case are chemical compounds. In *Juicy Whip Inc. v. Orange Bang, Inc.*, the issue of utility was discussed in regard to a juice dispenser, in *Brooktree Corp. v. Advanced Micro Devices, Inc.*, the issue of utility was discussed in regard to digital analog conversion circuitry, and in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.*, the issue of utility was discussed in regard to a business

method. Even assuming *arguendo* that all cited cases are relevant here, the claimed invention does not benefit the public in currently available form and therefore, does not satisfy the requirements of 35 USC § 101. As stated above, the claimed invention has no specific and substantial utility as the asserted utilities are applicable to the broad class of polynucleotides and/or require further experimentation to identify a "real world" use. It should be noted that in *Cross v Iizuka*, the specification disclosed the structure of the claimed imidazole derivative compounds and the specification provided experimental evidence of inhibition of thromboxane synthetase inhibition by these imidazole derivatives in human and bovine microsomes and a method for practicing such. In the instant case, the specification fails to provide guidance for practicing any patentable utility of the claimed sequences. Thus, in contrast to *Cross v Iizuka,* the claimed invention fails to benefit the public in currently available form.

At the top of page 14 of the response, applicants indicate that the requirements set forth in the Office action for compliance with 35 USC § 101 do not comply with the requirements set forth by the PTO itself for complying with 35 USC § 101. Applicants state that, while they are aware of the new utility guidelines set forth by the USPTO, the current rules and regulations are the patent laws set forth in 35 USC and the rules set forth in 37 CFR but not the MPEP or guidelines set forth by the USPTO. Applicants argue it is the job of the judiciary and not the USPTO to interpret these laws and rules. Applicants argue that they are unaware of recent changes in either 35 USC § 101 or in the interpretation of 35 USC § 101 by the Supreme Court or the Federal Circuit which support the new utility guidelines set forth by the USPTO. Applicants cite patents that allegedly do not contain examples of the "real world" utilities allegedly required by the Examiner. Applicants argue that holding them to a different standard of utility would be arbitrary and capricious.

Applicants are respectfully reminded that the examiner must examine a patent application according to the guidelines set forth by the USPTO as well as the MPEP, since the examiner has no authority to disregard such guidelines or to apply his own interpretation of patent law in the examination of the application. Furthermore, as set forth in the guidelines and the MPEP, the guidelines were promulgated by the PTO in accordance with all applicable case law and thus are believed to be consistent therewith. While the examiner acknowledges the cited US patents, each patent application is

examined on its own merits according to the current guidelines of examination as set forth by the USPTO and a discussion on the utility of any polynucleotide claimed in such patents would require a detailed review of the record of each individual case, which would be improper. Finally, applicants are further reminded that the examiner has no authority to comment in regard to the legality of the current utility guidelines or the MPEP as set forth by the USPTO.

Claim Rejections - 35 USC § 112, First Paragraph

[9] The enablement rejection of claims 1, 3-5, and 9-13 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item 20 of the Office action mailed June 09, 2003 and the reasons stated below. Applicants' arguments addressing the instant rejection are on page 15 of the response. Applicants argue the claimed invention has a specific, substantial, and credible utility and refer to their arguments addressing the utility rejection. It is the examiner's position that the claimed sequences do not have a specific and substantial utility or a well-established utility for the reasons set forth in the rejection under 35 USC § 101 above and applicants' arguments traversing the instant rejection have been fully addressed above.

[10] The written description rejection of claim 4 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth in item 21 of the Office action mailed June 09, 2003 and the reasons stated below. Applicants' arguments addressing the instant rejection begin at page 15 of the response. Applicants cite case law allegedly supporting a position that the specification adequately describes the claimed invention. Applicants argue that the claims at issue are in contrast to the claims of the *Lilly* and *Fiers* cases as the polynucleotides recited in the instant claims are not distinguished on the basis of function or a method of isolation, but are distinguished by structural features. Applicants argue that based on the sequences of the invention, one would be able to distinguish the claimed sequences from others based on the disclosed structural description. Applicants argue that nucleic acid molecules nucleotide sequences encoding SEQ ID NO:4 are encompassed by the genus of claim 4 and those that lack this requirement are not. Applicants' arguments are not found persuasive.

It is acknowledged that the current claims differ from the *Lilly* and *Fiers* cases. However, applicants have failed to address the issue at hand – whether the specification discloses a *representative number of species* to adequately describe the genus of claimed polynucleotides. The written description requirement for a claimed genus may be satisfied through sufficient description of *a representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicants were in possession of the claimed genus. A representative number of species means that the species that are adequately described are representative of the entire genus. When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. See MPEP § 2163. It is the examiner's position that the single disclosed representative species of SEQ ID NO:3 fails to adequately describe the claimed invention. As stated in a previous Office action (see page 10 of the Office action mailed June 09, 2003), SEQ ID NO:4 is only a fragment of a full-length polypeptide, and thus, the species encompassed by the genus of encoding nucleic acids of claim 4 reads on numerous undisclosed nucleic acids, including, *e.g.,* full-length genes, chromosomal DNA, and a variety of nucleic acids encoding proteins other than SEQ ID NO:4 or SEQ ID NO:2. In the instant case, the claimed genus of polynucleotides encompasses species that are widely variant in both structure and function, including (but not limited to) genomic and chromosomal sequences from any organism comprising the recited sequence, allelic variants, and nucleic acid variants encoding polypeptides having function other than the asserted protease inhibitor activity, e.g., non-functional polypeptides and polypeptides having activity other than the asserted protease inhibitor activity. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". As the claimed genus encompasses species that are widely variant in both structure AND function, the disclosure of the single representative species of SEQ ID NO:3 is insufficient to be representative of the attributes and features of *all* species

encompassed by the claimed genus of polynucleotides. In this case, applicants have failed to demonstrate that the specification discloses a representative number of species of the claimed genus of polynucleotides. Given the lack of description of a representative number of polynucleotides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

The examiner acknowledges applicants' remarks at the first full paragraph of page 17 of the response. Applicants' arguments appear to address the breadth and scope of the claimed subject matter. It is noted that the examiner has examined the claims in accordance with MPEP § 2111, which directs the examiner to give claims their broadest reasonable interpretation. As such, it is unclear to the examiner as to how the examiner's comments are "directly in contrast with the relevant case law", "are contradicted by the wealth of case law concerning claim scope", and are "erroneous". In order to clarify the record, the examiner requests that applicants provide supporting details of how the examiner's comments are "directly in contrast with the relevant case law", "are contradicted by the wealth of case law concerning claim scope", and are "erroneous" in order that the examiner may fully respond to applicants' assertions.

Conclusion

[11] Status of the claims:

- Claims 1, 3-5, and 9-13 are pending.
- Claims 1, 3-5, and 9-13 are rejected.
- No claim is in condition for allowance.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally

be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

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